

B1
m6
D1

1. (twice amended) A method for treating a cancer, comprising administering a compound that is a selective antagonist to an endothelin B receptor, to a patient in need thereof.

B2
m6
D17

14. (amended) A method for treating cancer, wherein the cancer cells express the endothelin B receptor, comprising administering a compound that is a selective antagonist to the endothelin B receptor to a patient in need of such treatment.

15. (amended) A method for treating cancer, comprising administering a compound that prevents the downregulation of E-cadherin in the cancer cell to a patient in need of such treatment.

REMARKS

Upon entry of the present amendments, Claims 1-5, 14 and 15 will be pending and under active consideration. Claims 1-5 are indicated to be free of prior art. A marked version of the claims indicating the changes to the claims is attached hereto as Appendix A. The amendments are fully supported by the present specification as mentioned below, and do not represent new subject matter.

Claims 1, 14 and 15 have been amended to recite patients as the subject of treatment rather than subjects. Support for use of the term "patient" can be found throughout the specification, particularly at page 18 lines 16-19, page 29 lines 17-21, and page 35 lines 27-29. Thus, the amendments to Claims 1, 14, and 15 are fully supported and do not constitute new matter.

The drawings are objected to by the draftsman. In response, corrected formal drawings are submitted under separate transmittal. Accordingly, this objection is obviated

1. **The Claimed Invention Is Not Anticipated Under 35 U.S.C. § 102 (e)**

Claim 14 is rejected under 35 U.S.C. § 102 (e) as anticipated by Vournakis et al., U.S. Patent number 6,063,911 (filed December 22, 1998). This rejection is obviated for reasons explained below.

Claim 14 has been amended to specify that the compound used in the claimed method is a selective antagonist of the endothelin B receptor. The amendment renders Claim 14 commensurate in scope with Claim 1 and claims dependent therefrom which have been found free of the art of record.

In view of the foregoing, the rejection under 35 U.S.C. § 102 (e) is obviated, and should be withdrawn.

2. Rejection Based on 35 U.S.C. § 112, Second Paragraph

Claims 1-5, 14, and 15 are rejected under 35 U.S.C. § 112, second paragraph, as indefinite for failing to particularly point and distinctly claim the subject matter which the Applicants regard as the invention. The Examiner contends that the use of the term "compound" is vague and indefinite. This rejection should be withdrawn for reasons detailed below.

The claims of the invention are directed to a method for treating cancer by administration of a compound having a particular property, i.e. being a selective antagonist of the endothelin B receptor. The claims are not vague or indefinite -- they precisely cover what is intended as the invention in its broadest sense -- the use of any compound that demonstrates the specified property -- i.e. selectivity for endothelin B receptor. In this regard, the specification discloses a number of novel compounds that are selective endothelin B receptor antagonists, that can be used in accordance with the claimed invention. See page 15 lines 15-31. Additional examples of selective compounds that can be used in the methods of the invention are listed in the specification at page 26 lines 9-20 and page 16 lines 1-27. Moreover, the specification explicitly states that the compounds that can be used in the methods of the invention are not limited to the specific examples disclosed, and describes assays that can be used to determine the specificity of candidate compounds for use in the method of the invention. Assays for identifying appropriate compounds can be based on selectively inhibiting endothelin B receptor activation or observing vasoconstrictor activity. *In vitro* assays described in section 2.2.1.1 of the specification include assays based on ¹²⁵I-labeled ET-1 binding in cardiovascular tissue, and measurement of the inhibition by cyclic peptides of ET-1 binding to ET-specific receptors. Melanocyte cells expressing endothelin B receptors can be used in cell culture assays. Additional assays are described in sections 5.6.1

and 5.6.2 which can be used for identifying compounds capable of selectively binding to target gene products of the invention and for identifying compounds that modulate the interaction between the target gene product and its cellular or extracellular binding partner(s). One of skill in the art can readily use the assays taught in the specification to determine whether a candidate compound has activity as a selective endothelin B receptor antagonist or not. This includes any compound yet to be discovered that has activity as a selective endothelin B receptor antagonist. As disclosed in the specification, any such compounds identified as selective endothelin B receptor antagonists can be employed in the method of the claimed invention. Therefore, the skilled artisan can obtain from the specification sufficient knowledge of the types of compounds that can be used in the methods of the claimed invention such that the methods are effective in treating cancer.

To answer the Examiner's question, "[h]ow would one know if the patented claim was being infringed?" The metes and bounds of the claims can clearly be determined. One of skill in the art could readily determine whether a compound has activity as a selective endothelin B receptor antagonist given the teachings of the specification, and as a result determine whether a compound is applicable for use in the claimed method. To re-iterate, assays to determine whether a compound is appropriate for use in the invention are described in sections 5.6.1 and 5.6.2 of the specification, particularly at page 45 line 24 through page 47 line 6. Thus, the knowledge required to determine the scope of the claimed methods lies in use of a selective endothelin B receptor antagonist for treating cancer rather than the specific type of compound employed for that purpose.

The present situation is analogous to the claims in Application of William L. Goffe 526 F.2d 1393 (CCPA 1975). In *Goffe*, the court reversed the Board of Appeals decision which supported the Examiner's rejection of a method claim based on indefiniteness of process step terms or limitations under 35 U.S.C. § 112, second paragraph. In its opinion, the court explained that the mere fact that a process step within the method claim covers the use of a large number of possible materials does not in and of itself render the claims indefinite, citing, In re Skoll, 523 F.2d 1392 (CCPA 1975). The issue is whether those skilled in the art could ascertain what falls within the scope of the method claims. In the present invention, the compounds to which the Examiner rejects are analogous to the materials of *Goffe*. As explained in detail above, given the teaching of the specification, one skilled in the art could

readily determine whether a compound has activity as a selective endothelin B receptor antagonist. Furthermore, the *Goffe* court stated, " The scope of the claims is definite because each of the limitations recited therein is definite. See *In re Wakefield*, 422 F.2d 897 (CCPA 1970)." The situation is analogous to that of the rejected claims of the present invention wherein the limitation (i.e. a compound that is a selective antagonist of the endothelin B receptor) is recited in the claims and is definite in light of the teachings of the specification as described above.

In view of the above remarks, the scope of the claimed subject matter, methods of treating cancer, can be determined by one having ordinary skill in the art. This rejection under 35 U.S.C. § 112 second paragraph, therefore, should be withdrawn.

CONCLUSION

The applicant respectfully requests entry of the amendments and remarks made herein into the file history of the present application.

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Respectfully submitted,

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APPENDIX A
MARKED-UP COPY OF THE AMENDED CLAIMS
(Filed March 5, 2002)
U.S. PATENT APPLICATION SERIAL NO. 09/305,084

1. (twice amended) A method for treating a cancer, comprising administering a compound that is a selective antagonist to an endothelin B receptor, to a patient in need thereof.

14. (amended) A method for treating cancer, wherein the cancer cells [selectively] express the endothelin B receptor, comprising administering a compound that is [an] a selective antagonist to [an] the endothelin B receptor to a [subject] patient in need of such treatment.

15. (amended) A method for treating cancer, comprising administering a compound that prevents the downregulation of E-cadherin in the cancer cell to a [subject] patient in need of such treatment.

APPENDIX B
THE CLAIMS WHICH WILL BE PENDING
UPON ENTRY OF THE PRESENT AMENDMENT
(Filed March 5, 2002)

U.S. PATENT APPLICATION SERIAL NO. 09/305,084

1. (twice amended) A method for treating a cancer, comprising administering a compound that is a selective antagonist to an endothelin B receptor, to a patient in need thereof.
2. The method of Claim 1 in which the cancer is selected from the group consisting of melanoma, prostate cancer, colon cancer, ovarian cancer or mammary cancer.
3. The method of Claim 2 in which the cancer is melanoma.
4. (twice amended) The method of Claim 1, in which the compound is a mimic of Endothelin-1 that binds to the endothelin B receptor.
5. (amended) The method of Claim 1 in which the compound is an antisense molecule that blocks translation of a polypeptide that activates the endothelin B receptor.
14. (amended) A method for treating cancer, wherein the cancer cells express the endothelin B receptor, comprising administering a compound that is a selective antagonist to the endothelin B receptor to a patient in need of such treatment.
15. (amended) A method for treating cancer, comprising administering a compound that prevents the downregulation of E-cadherin in the cancer cell to a patient in need of such treatment.